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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/016,283	11/30/2001	David M. Valenzuela	REG 195-BZ	9910

7590 08/25/2003

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EXAMINER	
LANDSMAN, ROBERT S	

ART UNIT	PAPER NUMBER
1647	5

DATE MAILED: 08/25/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	10/016,283	VALENZUELA ET AL.	
	Examiner	Art Unit	
	Robert Landsman	1647	

-- The MAILING DATE of this communication appears n the cover sheet with the correspondenc address --

Period f r Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 2 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 March 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *12-24,47,49-54,56,57,59,61 and 63-100* is/are pending in the application.

4a) Of the above claim(s) *12-24,47,49-54,56,57,59,61,63-84 and 98-100* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *85-97* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: Sequence Comparison

DETAILED ACTION

1. Election/Restriction

A. Claims 12-24, 38-47, 49-54, 56, 57, 59-61 and 63-84 were pending in the application and were subject to restriction as follows:

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 12-14, drawn to a method of promoting growth of a cell expressing a MuSK receptor by administering agrin, classified in class 435, subclass 7.2.

II. Claims 15-17 and 59, drawn to a MuSK antibody, classified in class 530, subclass 387.1

III. Claims 18-24, 49 and 63, drawn to a method of detecting agrin in a sample using an antibody, and a kit classified in class 435, subclass 7.1.

IV. Claims 38-46 and 60, drawn to a polypeptide encoding the active portion of human agrin, classified in class 530, subclass 350.

V. Claim 47 and 61 in part, drawn to the use of a polypeptide encoding agrin to manufacture a medicament, classified in class 514, subclass 2.

VI. Claims 50, 53 and 61 in part, drawn to a method of treating a patient by administering a nucleic acid encoding agrin, classified in class 514, subclass 44.

VII. Claims 51, 52, 54, 56 and 57, drawn to a nucleic acid molecule encoding human agrin, a vector and host cell classified in class 435, subclass 69.1.

VIII. Claims 64-68, drawn to a method of inducing AChR clustering on a muscle cell, classified in class 435, subclass 7.1.

IX. Claims 69-73, drawn to a method of inducing phosphorylation of MuSK, classified in class 435, subclass 7.1.

X. Claims 74 and 75, drawn to a method of facilitating binding of agrin to MuSK receptors, classified in class 435, subclass 7.1.

XI. Claims 76-78, drawn to a method of targeting muscle cells, classified in class 514, subclass 2.

XII. Claims 79-84, drawn to a method of modulating the activity of the MuSK receptor, classified in class 435, subclass 7.2.

B. The inventions are distinct, each from each other because of the following reasons:

Inventions I, III, VI, V, VIII-XII are independent and distinct, each from the other, because the methods are practiced with materially different process steps for materially different purposes and each method requires a non-coextensive search because of different starting materials, process steps and goals.

Invention I is unrelated to Inventions II, VII. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are not disclosed as capable of use together.

Inventions I and IV are related as product and processes of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product, or (2) the product as claimed can be used in a materially different process of using that product MPEP § 806.05(h). In the instant case the polypeptide can be used as antigen for antibody production.

Inventions II and III are related as product and processes of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product, or (2) the product as claimed can be used in a materially different process of using that product MPEP § 806.05(h). In the instant case the antibody can be used to purify a protein.

Inventions II, IV, VII are independent and distinct, each from each other, because they are products which possess characteristic differences in structure and function and each has an independent utility that is distinct for each invention which cannot be exchanged. The polynucleotide of invention VII can be used to make a hybridization probe, or can be used in gene therapy as well as to produce the protein of interest. The protein of invention IV can be used for purposes other than to make an antibody of Group II, such as a probe, or used therapeutically or diagnostically (e.g. in screening). The antibody of Group II can be used for reasons other than to obtain the protein of Group IV. For example, the antibody may be used in diagnostics (e.g. as a probe in immunoassays, or in immunochromatography), or therapeutically.

Invention II is unrelated to Inventions V, VI, VIII-XII. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are not disclosed as capable of use together.

Invention III is unrelated to Inventions IV, VII. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are not disclosed as capable of use together.

Inventions IV and V, VIII-XII are related as product and processes of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product, or (2) the product as claimed can be used in a materially different process of using that product MPEP § 806.05(h).

Invention IV is unrelated to Inventions VI. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are not disclosed as capable of use together.

Invention V is unrelated to Inventions VII. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are not disclosed as capable of use together.

Inventions VI and VII are related as product and processes of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product, or (2) the product as claimed can be used in a materially different process of using that product MPEP § 806.05(h). In the instant case, the nucleic acid can be used to produce a protein.

Invention VII is unrelated to Inventions VIII-XII. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are not disclosed as capable of use together.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification and recognized divergent subject matter as defined by MPEP § 808.02, the Examiner has *prima facie* shown a serious burden of search (see MPEP § 803). Therefore, an initial requirement of restriction for examination purposes as indicated is proper.

C. A telephone call was made to Linda Palladino on January 09, 2003 to request an oral election to the above restriction. Applicants elected Group IV, claims 38-46 and 60. However, Applicants cancelled these claims and added new claims 85-100. Applicants state that these new claims more clearly define the subject matter of the invention. However, claims 98-100 are method claims which correspond most closely with non-elected Groups VIII, XII and XI, respectively. Regardless, since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 98-100 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03. Therefore, claims 85-97 are the subject of this application. However, method claims that are commensurate in scope with the originally elected invention will be rejoined if the claims to said invention are found allowable and the rejoined claims do not contain any issues under 35 USC 112. This restriction is deemed proper and is, therefore, made **FINAL.**

The elected agrin protein (claims 85-97) and the method of using the protein are related as product and processes of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product, or (2) the product as claimed can be used in a materially different process of using that product MPEP § 806.05(h).

D. Applicant is reminded that upon cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR § 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a diligently-filed petition under 37 CFR § 1.48(b) and by the fee required under 37 CFR § 1.17 (h).

2. Specification

A. Figures 1, 4, 14 and 15 are objected to since the sequences are not identified by sequence identifiers (i.e. SEQ ID NO) in either the Figure itself or in the Brief Description of the Figures. While not being objected to, it is brought to Applicants' attention that Figure 12 is not labeled consistently with, for example, figures 1, 4 and 13, which recite, for example "12A" "12B" and "12C."

B. The specification is objected to since the continuing data in the first line of the specification must refer to any parent applications filed under 35 USC 120 as either a CIP, CON or DIV (i.e. 08/644,271).

C. While not being objected to, it is brought to Applicants' attention that the first line of the specification is inconsistent with the Bibliographic Data Sheet regarding the priority claims. The specification does not reference 09/077,955 nor PCT/US96/20696 (as does the Oath), whereas the Bibliographic Data Sheet does not reference 08/644,271 or 60/008,657. This issue may be handled now or the allowance of any patentable claims. However, a clarification of the priority would be appreciated.

3. Claim Rejections - 35 USC § 112, first paragraph – enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

A. Claims 85-97 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the protein of SEQ ID NO:36, does not reasonably provide enablement for any human agrin protein, modified forms, or fragments thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

In In re Wands, 8USPQ2d, 1400 (CAFC 1988) page 1404, the factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

First, the breadth of the claims is excessive with regard to claiming all human agrin proteins capable of inducing phosphorylation of "**any and all MUSK proteins**", or for the use of "**fragments**" and proteins with one or more amino acid "**deletions and/or insertions**" to human agrin. Protein fragments or those with deletions and/or insertions would have one or more amino acid deletions or insertions to the full-length agrin protein of SEQ ID NO:36, or to any full-length agrin protein. In addition, various MUSK proteins would also have one or more amino acid additions, substitutions, deletions or insertions to the MUSK of the invention and Applicants do not provide any guidance on how to identify a MUSK, or the genus of MUSK proteins.

Applicants only provide guidance or working examples of the agrin protein of SEQ ID NO:36 and one MUSK protein. Applicants have not provided any guidance or working examples of any other human agrin proteins, or of any and all MUSK proteins, nor have they provided guidance or working examples of any proteins other than the full-length agrin protein of SEQ ID NO:36. Applicants have not taught which fragments of human agrin can be altered and still retain its ability to bind MUSK, nor have they taught which amino acids can be deleted or inserted and still retain the function of agrin or MUSK. Furthermore, it is not predictable to one of ordinary skill in the art what amino acids can be altered in either agrin or MUSK in order to retain the desired characteristics.

In summary, the breadth of the claims is excessive with regard to Applicants claiming all human agrin and MUSK proteins, or fragments of agrin having additions or deletions, other than that of the full-length agrin of SEQ ID NO:36, or the MUSK of the invention. Furthermore, Applicants have not provided any guidance or working examples of these proteins. These factors, along with the lack of predictability to one of ordinary skill in the art as to how to make functional agrin and MUSK other than those disclosed in the specification leads the Examiner to hold that undue experimentation is necessary to practice the invention as claimed.

4. Claim Rejections - 35 USC § 112, first paragraph – written description

A. Claims 85-97 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

These are genus claims. Agrin fragments or those with deletions and/or insertions to SEQ ID NO:36 would have one or more amino acid deletions or insertions to the full-length agrin protein of SEQ ID NO:36, or to any full-length agrin protein. In addition, various MUSK proteins would also have one or more amino acid additions, substitutions, deletions or insertions to the MUSK of the invention and Applicants do not adequately describe the MUSK or agrin genus.

The specification and claims do not indicate what distinguishing attributes are shared by the members of the genus. Thus the scope of the claims includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted. The specification and claims do not provide any guidance as to what changes should be made. Structural features that could distinguish compounds in the genus from others in the protein class are missing from the disclosure. No common structural attributes identify the members of the genus. The general knowledge and level of skill in the art do not supplement the omitted description because specific,

not general, guidance is what is needed. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, "human agrin," "MUSK," or "SEQ ID NO:36" alone are insufficient to describe the genus. One of skill in the art would reasonable conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, Applicant was not in possession of the claimed genus at the time the invention was made.

5. Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

A. Claim 90 recites the limitation "four amino acids." There is insufficient antecedent basis for this limitation in the claim. Claim 89, from which claim 90 depends, recites "8 amino acids.

B. Claim 96 is confusing since it is not clear what the metes and bounds of "accessory componenet" are.

6. Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

A. Claims 85-87, 89 and 93-96 are rejected under 35 U.S.C. 102(b) as being anticipated by Rupp et al. (J/ Neuroscience). The claims recite a fragment of human agrin, or an agrin having one or more amino acid deletions or insertions. Rupp et al. teach an agrin protein which is 82% identical to SEQ ID NO:36 (Sequence Comparison). Though Rupp do not teach a human agrin, the claims do not require that the protein be a human agrin. Claim 85 recites a fragment of human agrin capable of phosphorylating MUSK. The protein of Rupp has numerous fragments identical to that of the present invention. In absence of evidence to the contrary it would be expected that one or more of the fragments of the protein of Rupp would phosphorylate MUSK. In addition, claims 86, 87 and 89 recite that the protein has numerous deletions, though not necessarily of contiguous residues. Since the claims recite "A human agrin protein

having deletions," the protein of Rupp would meet this limitation since it, in fact, has these deletions and, though not a human protein, would still be identical to a human protein having deletions. The artisan would immediately envision agrin in a pharmaceutical composition. Furthermore, buffers are taught, or are inherent in the methods seen on page 3536.

7. Conclusion

A. No claim is allowable.

Advisory information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert Landsman whose telephone number is (703) 306-3407. The examiner can normally be reached on Monday - Friday from 8:00 AM to 5:00 PM (Eastern time) and alternate Fridays from 8:00 AM to 5:00 PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623.

Official papers filed by fax should be directed to (703) 308-4242. Fax draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Robert Landsman, Ph.D.
Patent Examiner
Group 1600
August 22, 2003

ROBERT LANDSMAN
PATENT EXAMINER

Sequence Comparison

C;Species: Rattus norvegicus (Norway rat)
C;Date: 31-Mar-1993 #sequence_revision 31-Mar-1993 #text_change 17-Nov-2000
C;Accession: JH0399; A38856
R;Rupp, F.; Payan, D.G.; Magill-Solc, C.; Cowan, D.M.; Scheller, R.H.
Neuron 6, 811-823, 1991
A;Title: Structure and expression of a rat agrin.
A;Reference number: JH0399; MUID:91222570; PMID:1851019
A;Accession: JH0399
A;Molecule type: mRNA
A;Residues: 1-1779;1799-1959 <RUP>
A;Cross-references: GB:M64780; NID:g202798; PIDN:AAA40703.1; PID:g202800
A;Experimental source: embryonic spinal cord
A;Note: it is uncertain whether Met-1, Met-18, or Met-24 is the initiator
R;Rupp, F.; Oezcelik, T.; Linial, M.; Peterson, K.; Francke, U.; Scheller, R.
J. Neurosci. 12, 3535-3544, 1992
A;Title: Structure and chromosomal localization of the mammalian agrin gene.
A;Reference number: A38856; MUID:92407628; PMID:1326608
A;Accession: A38856
A;Molecule type: mRNA
A;Residues: 1780-1798 <RU2>
A;Cross-references: GB:S44194
C;Comment: This protein mediates the motor neuron-induced aggregation of acetylcholine receptors and acetylcholine-esterase on the surface of muscle fibers of the neuromuscular junction.
C;Comment: 90% of rat embryonic transcripts encode the variant labeled below as form 3. However, alternative splicing may produce as many as eight different forms of agrin, which differ in their acetylcholine receptor clustering activity.
C;Superfamily: agrin; EGF homology; Kazal proteinase inhibitor homology; laminin G repeat homology; laminin-type EGF-like homology
C;Keywords: alternative splicing; duplication; glycoprotein; neuromuscular junction
F;1-1959/Product: agrin, form 1 #status predicted <AG1>
F;1-1787,1799-1959/Product: agrin, form 4 #status predicted <AG4>
F;1-1779,1799-1959/Product: agrin, form 3 #status predicted <AG3>
F;1-1779,1788-1959/Product: agrin, form 5 #status predicted <AG5>
F;1-1143,1153-1959/Product: agrin, form 2 #status predicted <AG2>
F;22-50/Region: hydrophobic
F;88-137/Domain: Kazal proteinase inhibitor homology <KPI1>
F;163-212/Domain: Kazal proteinase inhibitor homology <KPI2>
F;236-284/Domain: Kazal proteinase inhibitor homology <KPI3>
F;307-356/Domain: Kazal proteinase inhibitor homology <KPI4>
F;381-429/Domain: Kazal proteinase inhibitor homology <KPI5>
F;446-494/Domain: Kazal proteinase inhibitor homology <KPI6>
F;511-559/Domain: Kazal proteinase inhibitor homology <KPI7>
F;540-542/Region: motor neuron attachment (L-R-E) motif
F;596-645/Domain: Kazal proteinase inhibitor homology <KPI8>
F;688-739/Domain: laminin-type EGF-like homology <LE1>
F;742-786/Domain: laminin-type EGF-like homology <LE2>
F;814-864/Domain: Kazal proteinase inhibitor homology <KPI9>
F;869-992/Region: serine/threonine-rich
F;1084-1086/Region: motor neuron attachment (L-R-E) motif
F;1147-1215/Region: serine/threonine-rich
F;1224-1257/Domain: EGF homology <EG1>
F;1287-1442/Domain: laminin G repeat homology <LG1>
F;1444-1476/Domain: EGF homology <EG2>
F;1483-1515/Domain: EGF homology <EG3>
F;1555-1706/Domain: laminin G repeat homology <LG2>
F;1713-1747/Domain: EGF homology <EG4>
F;1807-1959/Domain: laminin G repeat homology <LG3>
F;97-116,105-137,171-191,180-212,244-263,252-284,316-335,324-356,389-408,397-429,454-473,462-494,518-538,527-559,604-624,613-645,823-843,832-864,1224-1235,1229-1246,1248-1257,1444-1455,1449-1465,1467-1476,1483-1494,1488-1504,1506-1515/Disulfide bonds: #status predicted
F;145,672,827,957/Binding site: carbohydrate (Asn) (covalent) #status predicted

Query Match 82.2%; Score 2127.5; DB 1; Length 1959;
Best Local Similarity 83.8%; Pred. No. 2e-149;
Matches 404; Conservative 22; Mismatches 45; Indels 11; Gaps 1;

```
Qy         22 DKKSPCQPNPCHGAAPCRVLPEGGAQCECPLGREGTFCQTASGQDGSGPFLADFNGFSHL 81
              |:||||||||||||||||||  |||:|||||||  ||||||     ||  ||||||||||:|
Db       1478 DEKSPCQPNPCHGAAPCRVLSSGGAKCECPLGRSGTFCQTVLETAGSRPFLADFNGFSYL 1537

Qy         82 ELRGLHTFARDLGEKMALEVVFLARGPSGLLLYNGQKTDGKGDFVSLALRDRRLEFRYDL 141
              ||:|||||  ||||||||||:|||||||||||||||||||||||||||||  :|  |||  |||
Db       1538 ELKGLHTFERDLGEKMALEMVFLARGPSGLLLYNGQKTDGKGDFVSLALHNRHLEFCYDL 1597

Qy        142 GKGAAVIRSREPVTLGAWTRVSLERNGRKGALRVGDGPRVLGESPKSRKVPHTVLNLKEP 201
              |||||||||:||: || | || ||||||||||:||||||||||||||||||||:||||||
Db       1598 GKGAAVIRSKEPIALGTWVRVFLERNGRKGALQVGDGPRVLGESPKSRKVPHTMLNLKEP 1657

Qy        202 LYVGGAPDFSKLARAAAVSSGFDGAIQLVSLGGRQLLTPEHVLRQVDVTSFAGHPCTRAS 261
              ||:||||||||||| ||||||| | |||||| | |||| |||||  |||:  || ||||:|
Db       1658 LYIGGAPDFSKLARGAAVSSGFSGVIQLVSLRGHQLLTQEHVLRAVDVSPFADHPCTQAL 1717

Qy        262 GHPCLNGASCVPREAAYVCLCPGGFSGPHCEKGLVEKSAGDVDTLAFDGRTFVEYLNAVT 321
              |:||||| ||||||| | ||||||||| |||||||||| ||::|||||||::||||||
Db       1718 GNPCLNGGSCVPREATYECLCPGGFSGLHCEKGLVEKSVGDLETLAFDGRTYIEYLNAVI 1777

Qy        322 ESELANEIPV----------EKALQSNHFELSLRTEATQGLVLWSGKATERADYVALAI 370
              ||||  ||||           |||||||||||||||||||||| |||  |||||:||||
Db       1778 ESELTNEIPAPETLDSRALFSEKALQSNHFELSLRTEATQGLVLWIGKAAERADYMALAI 1837

Qy        371 VDGHLQLSYNLGSQPVVLRSTVPVNTNRWLRVVAHREQREGSLQVGNEAPVTGSSPLGAT 430
              |||||||||:||||||||||| ||||||||: |||| ||||||||||||||||||||||
Db       1838 VDGHLQLSYDLGSQPVVLRSTVKVNTNRWLRIRAHREHREGSLQVGNEAPVTGSSPLGAT 1897

Qy        431 QLDTDGALWLGGLPELPVGPALPKAYGTGFVGCLRDVVVGRHPLHLLEDAVTKPELRPCP 490
              |||||||||||||  :|||| ||||||||||||||||||   ||||||||||||||||||
Db       1898 QLDTDGALWLGGLQKLPVGQALPKAYGTGFVGCLRDVVVGHRQLHLLEDAVTKPELRPCP 1957

Qy        491 TP 492
              ||
Db       1958 TP 1959
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